Polychlorinated Biphenyls in Breast Milk: Application of a PBPK Model for Site Specific Evaluations

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Abstract

Background: A mechanism to predict breast milk PCB concentrations, based on a mother's PCB exposure, is desirable for risk assessors and public health practitioners. This poster describes data from comparisons of a three-compartment physiologically-based pharmacokinetic (PBPK) model, and a one-compartment first order kinetic model for estimating breast milk PCB concentrations.

Methods: The PBPK model was modified from a recently described PBPK model; the one compartment first order kinetic model is used for traditional risk assessments. Model runs considered: 1) milk and blood PCB levels associated with specific fish consumption exposures; 2) the dose of PCB associated with a given PCB concentration in milk or blood; and 3) reductions in blood and milk PCB levels that result from dietary interventions to reduce exposures.

Results: A variety of model applications illustrate the capabilities for assessing temporal and media-specific PCB exposures. Model simulations indicate that PCB levels in milk are highest initially, and are reduced over a 6-month nursing period. Modeled data suggest that early-life interventions can have a significant effect on PCB levels in human milk. Simulation results from the PBPK and the one compartment models indicate the two models produce estimates that compared favorably.

Conclusions: Both models facilitate the evaluation of multiple site-specific exposure scenarios and permit a focused analysis of critical exposure questions. The PBPK model aids the evaluation of exposures on a temporal basis. A clarified view of exposures and related risks will also inform risk mitigation/remediation decisions at known hazardous waste and spill sites.

Background/Methods

Models were used to estimate the PCB153 concentrations expected in breast milk and blood of women eating PCB contaminated fish. Model-generated data for a Physiologically-Based Pharmacokinetic Model (PBPK) and a one-compartment pharmacokinetic model were compared.

FIGURE 1 Conceptual Illustration of the Two Models

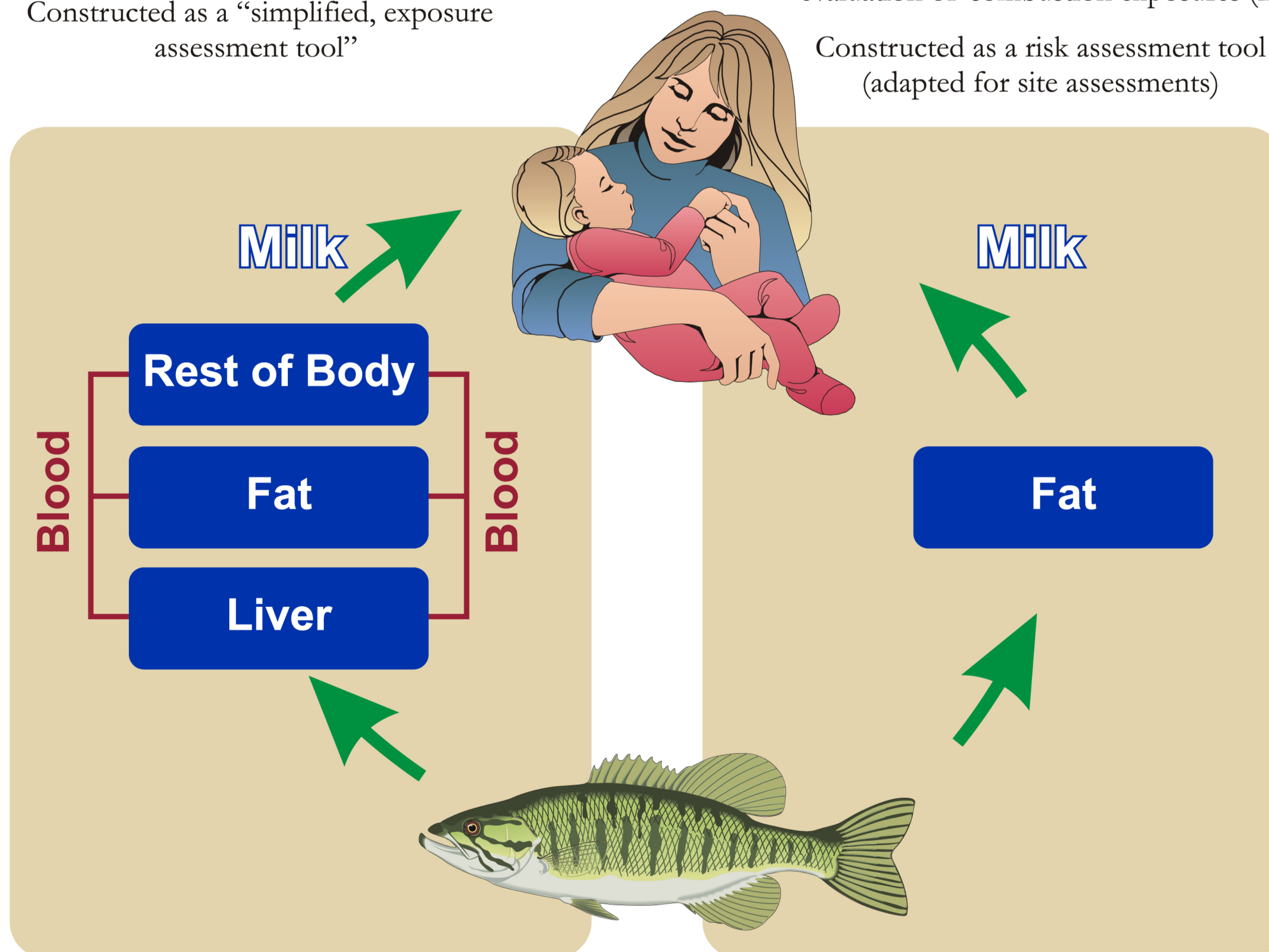**Physiologically-Based Pharmacokinetic Model (PBPK)**

Based on a previously published model (1)

Constructed as a "simplified, exposure assessment tool"

One-compartment pharmacokinetic model

Based on a model for EPA guidance for evaluation of combustion exposures (2)

Constructed as a risk assessment tool (adapted for site assessments)

Both models consider eating contaminated fish as the environmental exposure pathway.
Both models considered two exposure scenarios.
Both models considered lactating mothers previously exposed to PCB.

Mother's body weight is 64 kg
Mother's ingestion rate is 18 g of fish /day
Mother's exposure time is 25 years

Exposure 1) Fish at 1 mg PCB153 / kg   (PCB153 at 1 ppm)
       exposure dose of 281ng PCB153 / kg BW / day   (see Figure 2)

Exposure 2) Fish at 0.032 mg PCB153 / kg   (PCB153 at 0.032 ppm)
       exposure dose of 8.8 ng PCB153 / kg BW / day   (see Figure 2)

Typical Modeled Estimates

Given a fish consumption exposure: what are the predicted blood and human milk levels?

FIGURE 2
Estimated PCB153 in Blood and Breast Milk from Fish Eating
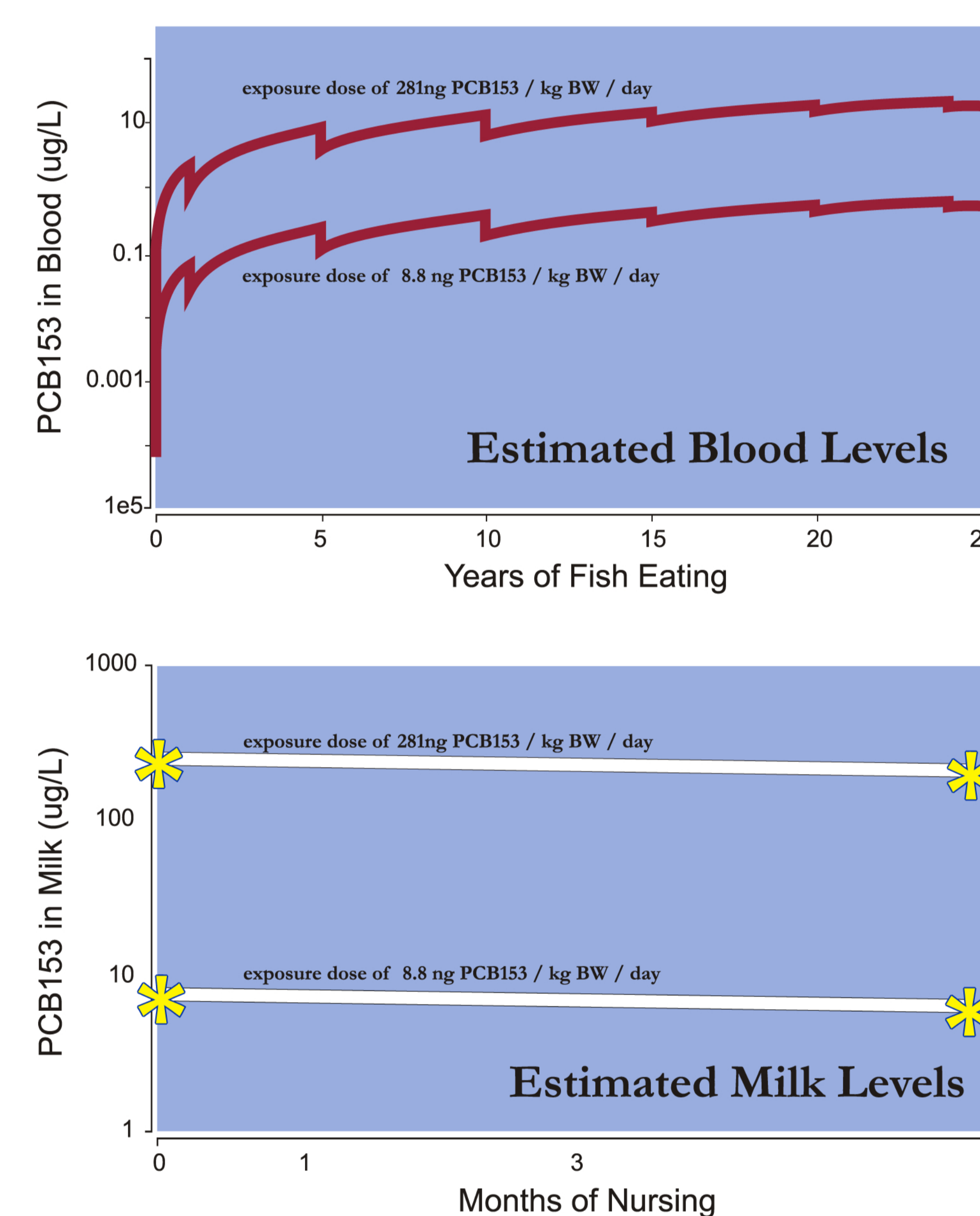
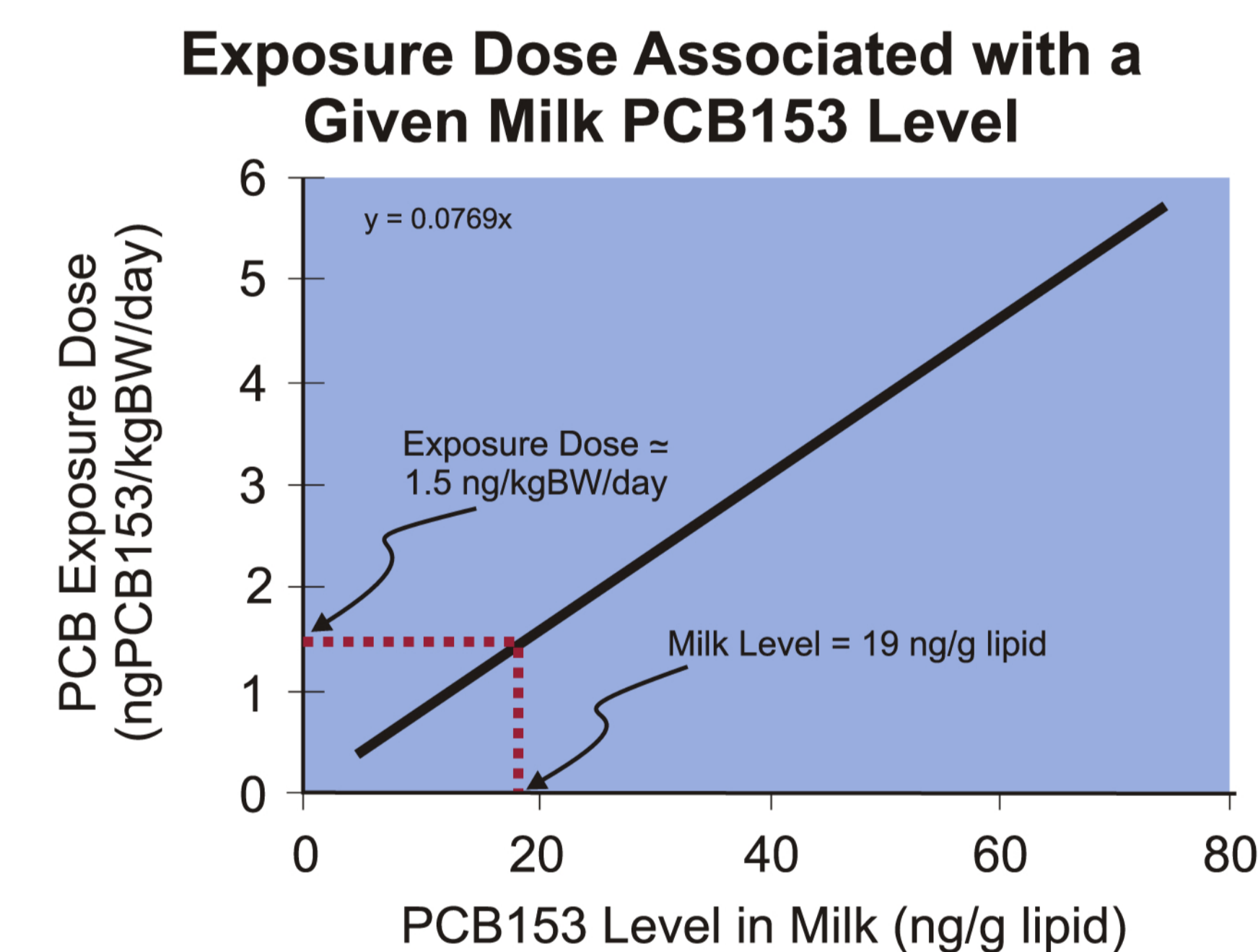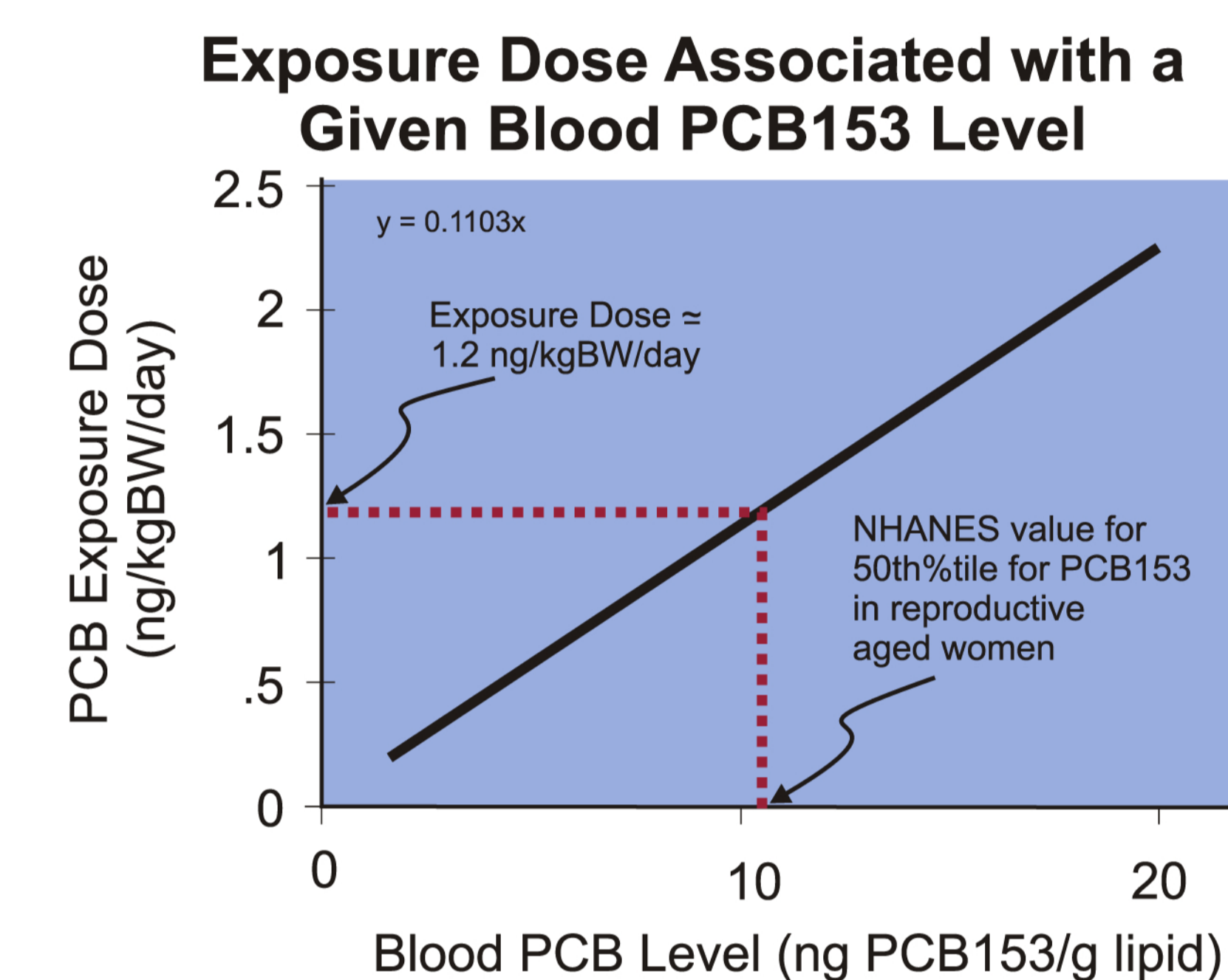
Point estimate from one compartment model noted with ✳

Notes: 25 year-old, 64 kg woman exposed to given dose of PCB153 for 25 years
    exposure dose of 281ng PCB153 / kg BW / day
    exposure dose of 8.8 ng PCB153 / kg BW / day

Reverse Dosimetry

Given blood or human milk levels: what is the predicted fish consumption exposure?

FIGURE 3
Estimated Exposure Doses to the Mother from Fish Consumption

Exposure Dose Associated with a Given Blood PCB153 Level

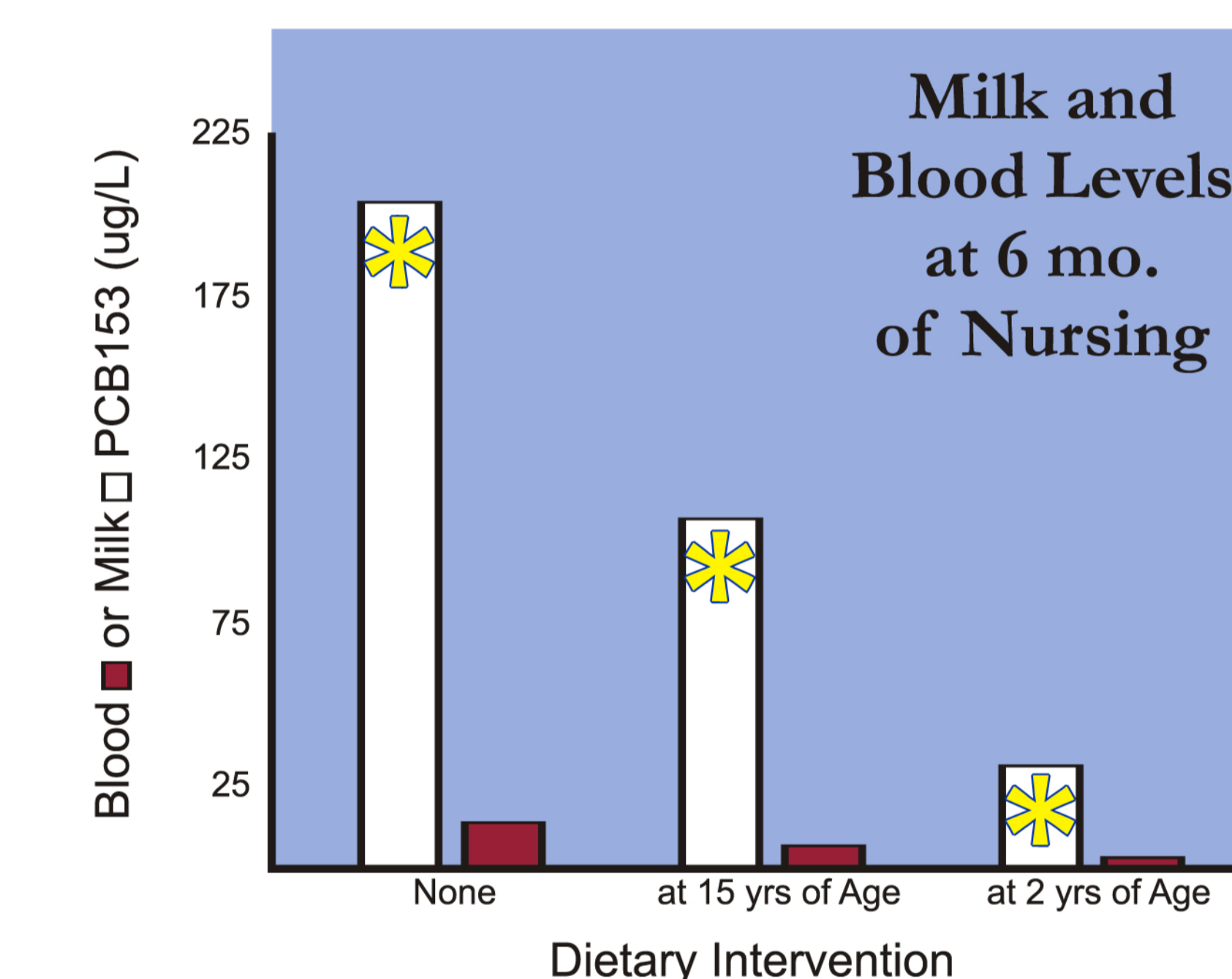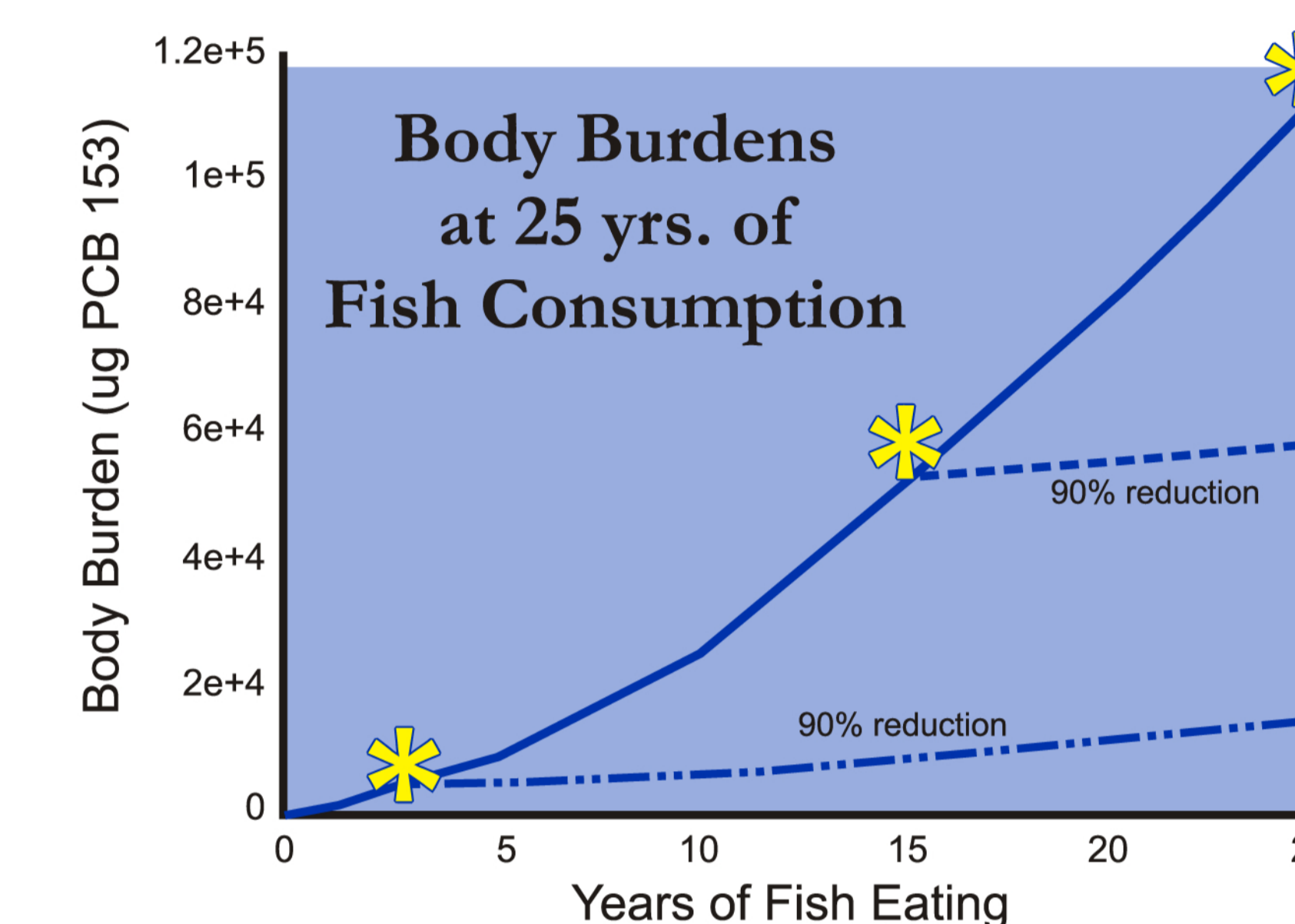**Exposure Dose Associated with a Given Milk PCB153 Level**

Exposure Dose is to Mother

Note: 25 year-old, 64 kg woman exposed to given dose of PCB153 for 25 years
NHANES data from reference 3.

Intervention Dosimetry

Given a dietary intervention: what exposure reductions are achieved?

FIGURE 4
Estimated Reductions in PCB153 Levels Due to Dietary Interventions

Point estimate from one compartment model noted with ✳

Notes: Dietary interventions were modeled to produce a 90% reduction in PCB153 ingestion at either 2 years of age, or 15 years of age
    exposure dose of 281ng PCB153 / kg BW / day

Conclusions

1. The models generate data that compare favorably and both models can be used to address a variety exposure-related questions.

2. If blood or milk PCB levels are available, modeled estimates of the associated exposure doses can add perspective to site-related exposure assessments.

3. The modeled data suggest that early-life interventions designed to reduce exposures can have dramatic effects on the levels of PCB in breast milk that is produced later stages in life.

Notes/References

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

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Conversions between units of ug/L and ng/g lipid were constructed using data and factors from references 3, 4, 5.

REFERENCES
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